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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,797	12/04/2001	John David Fraser	55503-002001	9884

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OCCHIUTI ROHLICEK & TSAO, LLP
10 FAWCETT STREET
CAMBRIDGE, MA 02138

EXAMINER	
JUEDES, AMY E	
ART UNIT	**PAPER NUMBER**
1644	

NOTIFICATION DATE	DELIVERY MODE
11/16/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@ORTPATENT.COM

Office Action Summary	Application No.	Applicant(s)	
	10/006,797	FRASER ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6,10,11,13,15-18,21-26,28-38 and 40-50* is/are pending in the application.

4a) Of the above claim(s) *17,18,21-26 and 28-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-6,10,11,13,15,16 and 40-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 9/14/10, are acknowledged.

Claims 2, 17, 21, and 26 have been amended.

Claims 46-50 have been added.

Claims 2-6, 10-11, 13, 15-18, 21-26, 28-38, and 40-50 are pending.

2. Claims 17, 18, 21-26 and 28-38 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 2-6, 10-11, 13, 15-16, and 40-50 are being acted upon.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 2-5, 10-11, 13, and 15-16 are rejected and claims 46 and 48 are rejected under 35 U.S.C. 102(a) as being anticipated by Hayball et al., Feb. 2000., as evidenced by Bannantine et al., 2004, and Invitrogen product information, 2008.

Hayball et al. teach a SEB superantigen with a mutation in the T cell receptor contact site (see page 13, in particular). Hayball et al. each that the superantigen is fused to polyhistidine (i.e. a protein/peptide antigen, see page 14, in particular). Hayball et al. teach that the superantigen fusion protein bind to MHC class II (see page 16, in particular). Additionally, SEB is a superantigen from *Staphylococcus aureus* (see page 14, in particular). Hayball et al. teach that the mutation in the TCR binding site is a deletion (see page 14, in particular). Hayball et al. teach that the SEB fusion protein is produced in a pTrcHis vector. As evidenced by Invitrogen product information, the pTrcHis vector contains a cleavage site for removal of polyhistidine (i.e. the polyhistidine is "reversibly" coupled). Furthermore, as evidenced by Bannantine et al., polyhistidine is non-immunogenic (see page 113, in particular). Additionally, Hayball et al. teach the superantigen conjugate as part of a composition suitable for incubation with cells, including as part of a composition comprising a 0.1% BSA/PBS solution (i.e. a pharmaceutically acceptable carrier, see page 14, in particular). Additionally, the recitation of a "vaccine" in claim 16 refers to an intended use of the claimed superantigen. The superantigen/His fusion protein of Hayball et al. is structurally identical to that of the instant claims, and would function as a "vaccine".

Applicant's arguments filed 9/14/10 have been fully considered, but they are not persuasive.

Applicant argues that claim 2 is limited to a conjugate designed for eliciting an immune response specific to the antigen to prevent or treat an infection or disorder. Applicant argues that it follows that the antigen must have certain significance to the infection or disorder, and that the polyhistidine of Hayball is not equivalent to the antigen of the instant claims.

The instant specification does not define the term "antigen" . However, on page 3, the specification discloses that the antigen is a protein, and can be entirely non-immunogenic . The polyhistidine tag of Hairball et al. is a protein. Furthermore, in response to Applicant's arguments, it is noted that under the appropriate circumstances, polyhistidine can function as an antigen since polyhistidine specific antibodies are known in the art (see Sood et al., 2000, page 283, right column, first full paragraph). Thus, polyhistidine can be considered an "antigen' as recited in the instant claims. Regarding the limitation that the conjugate elicit an immune response specific to the antigen to prevent or treat an infection or disorder, it is noted that this refers to an intended use of the claimed conjugate and does not carry patentable weight in the absence of a structural difference. The instant claims broadly encompass any antigen and are not limited to antigens related to a particular disease (such as a tumor antigen or antigen of a pathogen). Thus, the conjugate of Hayball et al. is structurally identical to that of the instant claims.

5. The following are new grounds of rejection necessitated by Applicant's amendment.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2-6, 10-11, 13, 15-16, and 40-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A conjugate comprising an antigen and a mutated superantigen having one or more mutations only in its T cell binding site, wherein said conjugate is capable of binding to a class II MHC molecule and eliciting an immune response specific to the antigen, a conjugate comprising a tumor antigen and a mutated superantigen having one or more mutations only in its T cell binding site, wherein said conjugate is capable of binding to a class II MHC molecule and eliciting an immune response specific to the tumor antigen to treat neoplastic diseases, and a conjugate comprising an antigen of a pathogen and a mutated superantigen having one or more mutations only in its T cell binding site, wherein said conjugate is capable of binding to a class II MHC molecule and eliciting an immune response specific to the antigen to treat an infection with the pathogen,

does not reasonably provide enablement for:

A conjugate comprising an antigen and a mutated superantigen having one or more mutations only in its T cell binding site, wherein said conjugate is capable of binding to a class II MHC molecule and eliciting an immune response specific to the antigen to prevent or treat an infection or disorder,

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely

related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The specification provides insufficient guidance to enable the skilled artisan to use the conjugate as broadly claimed, to prevent or treat an infection or disorder. As an initial matter, it is noted that the term "prevent", given its broadest reasonable interpretation, encompasses a complete prevention such that no signs or symptoms of disease ever develop. For example, "preventing" infection encompasses the prevention of a single cell from ever becoming infected with a pathogen. The ability to completely "prevent" diseases or infections is highly unpredictable, and the instant specification does not provide any examples or guidance demonstrating the effectiveness of the claimed conjugates for prevention of any disease.

Furthermore, the instant claims encompass using the claimed conjugates for eliciting an immune response specific for any antigen to treat any disorder. This might encompass using the claimed conjugates to treating a broad range of diseases or conditions mediated by completely different pathological mechanisms, including cancer, infection, autoimmune disease, heart disease, etc. For example, the claims might encompass using the conjugates to treat Alzheimer's disease. However, the role of inflammatory immune response in Alzheimer's disease is extremely complex and unpredictable, and the complexity makes it difficult to isolate any particular immune inflammatory process and pinpoint its individual role in the disease process (see Zotova et al., 2010). Thus, using a superantigen conjugate to induce an antigen specific immune response for treating Alzheimer's disease is highly unpredictable. Additionally,

the claims specifically encompass a conjugate comprising an autoantigen for treating autoimmune disease. Autoantigen administration for treating autoimmune disease is highly complex. For example, autoantigen administration can induce disease, under certain circumstances. Furthermore, treating disease with autoantigens require a specific type of immune modulation, such as reduction in T cell proliferation (see Blanas et al., 1996). Thus, using a conjugate comprising an autoantigen for treating autoimmune disease is highly unpredictable. Additionally, while tumor antigens and antigens form pathogens are known in the art and are capable of inducing an antigen specific immune response for treating tumors or infections, respectively, the instant claims encompass using a conjugate comprising any antigen for treating any disease (i.e. there is no requirement that the antigen be related to the disease to be treated). In fact, dependent claim 49 specifically encompasses using a whole viral antigen for treating the range of disease recited in claim 46, including tumors, autoimmune disease, or allergies.

Thus, given the unpredictability of the art and the breadth of the claims, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The instant specification demonstrates that immunization with a TCR mutated superantigen peptide conjugate is more effective for inducing peptide specific immune response than immunization with the peptide alone. Thus, it is conceivable that known tumor antigens or infectious antigens that are used to treat tumors or infections could be conjugated to the claimed superantigens for enhancing the antigen specific immune response for treating tumors or infections. However, the instant specification does not provide sufficient guidance to enable the skilled artisan to use the claimed conjugates to treat other disorders, such as allergy and autoimmune disease. No guidance regarding autoantigen/allergen selection, the route of administration, or the desired type of immune response is provided. Given the state of the art, it is not apparent how a conjugate that enhances T cell proliferation responses could be useful for treating autoimmune disease or allergy, which is mediated by aberrant autoantigen/allergen specific T cell responses. Furthermore, the instant specification does not provide any guidance regarding the use of non-specific antigens

for treating diseases (for example, using a viral antigen for treating tumors or autoimmune disease). Additionally, the instant specification does not provide any evidence that prevention of disease with the claimed conjugates is feasible. Thus, given the unpredictability of the art and the lack of guidance provided by the instant specification, it would require undue experimentation to use the conjugates as broadly claimed.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 46-48, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,968,514 (of record).

The '514 patent teaches a superantigen fragment (i.e. a mutated superantigen) that binds to MHC class II (i.e. is an APC targeting molecule, see abstract and column 5, in particular). The '514 patent teaches that said superantigen does not activate T cells, and inhibits T cells activated by the wild type superantigen (i.e. the T cell receptor binding site is deleted, see column 12, in particular). The '514 patent teaches conjugates comprising the mutated superantigen and tetanus toxoid (i.e. a bacterial antigen which comprises MHC class I and class II restricted peptides, see column 21, in particular). The '514 patent teaches using the conjugates as a vaccine to treat infections (see column 15, in particular).

Thus, the reference clearly anticipates the invention.

It is noted that claim 2 is being included in the above rejection, since new dependent claims 46-48 and 50 necessarily include all the limitations of claim 2.

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amy E. Juedes
Patent Examiner
Technology Center 1600
/Amy E. Juedes/
Primary Examiner, Art Unit 1644